

AMENDMENTS TO THE CLAIMS

This Listing of Claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1-18. (Canceled)

19. (Currently amended) A method of isolating a plurality of cells, wherein a subset of the cells ~~express~~expresses an RNA that is not expressed by another subset of the cells, comprising the steps of:

introducing into cells a plurality of ~~DNA that results in the expression of~~DNAs encoding a plurality of ~~endogenous RNA different RNAs~~, wherein ~~at least a subset of the plurality of endogenous RNA are different from each other~~each DNA further encodes a nucleic acid tag sequence, and wherein at least a subset of the plurality of DNAs encodes the same nucleic acid tag sequence;

exposing the cells to a ~~plurality of different signaling probes, wherein the signaling probes produce same signaling probe that produces~~ a detectable signal upon hybridization to ~~one or more RNAs of the plurality of endogenous RNA~~said same nucleic acid tag sequence; and

isolating the cells that produce the signal.

20. (Canceled)

21. (Currently amended) The method of claim 19, wherein the plurality of ~~RNA form~~

different RNAs forms an expression library.

22-24. (Canceled)

25. (Currently amended) The method of claim ~~4~~ or 19, further comprising the step of:

(a) culturing the isolated cells; or

(b) generating a plurality of cell lines by culturing the isolated cells.

26-33. (Canceled)

34. (Currently amended) The method of claim 19, wherein said plurality of DNAs encodes at least one ~~A method of isolating cells with reduced expression of a protein comprising the steps of:~~

~~introducing into cells a DNA encoding an antisense RNA, or an shRNA, or siRNA that reduces expression of said protein;~~

~~exposing the cells to a signaling probe that produces a detectable signal upon hybridization to said antisense RNA or shRNA; and~~

~~isolating the cells that produce the signal.~~

35-45. (Canceled)

46. (Currently amended) A ~~cell obtained~~ plurality of cells obtainable by the method of claim ~~4~~ or 19.

47-48. (Canceled)

49. (Currently amended) The ~~cell~~plurality of cells of claim 46, wherein the ~~cell is an~~cells
are embryonic stem ~~cell~~cells.

50. (Currently amended) A method for generating a transgenic or chimeric animal
comprising the step of using ~~the~~an embryonic stem cell of claim 49 to produce said
transgenic or chimeric animal.

51-102. (Canceled)

103. (Currently amended) A library of ~~mammalian~~ cell lines ~~comprising at least 1,000 cell~~
~~lines each comprising a stably integrated expressed sequence generated by growing the~~
plurality of cells of claim 46.

104-108 (Canceled)

109. (Currently amended) The library of claim 103, wherein ~~each cell line comprises at least~~
two of said cell lines comprise a variable library sequence.

110. (Currently amended) The library of claim 109, wherein the variable sequence of said
~~expression~~ library is selected from the group consisting of genomic, genomic

untranslated, genomic translated, gene, cDNA, EST, oligo, random, RNA, protein, protein domain, peptide, intronic, exonic, tag, or linker sequence, or combination thereof or recombination thereof, or one or more of the unmodified, mutagenized, randomized, shuffled or recombined sequences.

111-113. Canceled.

114. (Currently amended) A method of using the ~~The~~ library of claim 103, ~~wherein the library is used~~ in a cell-based screening assay.

115-116. (Canceled).

117. (New) The method of claim 19, further comprising separately growing individually isolated cells to generate a plurality of separate cell lines.

118. (New) The method of claim 19, further comprising pooling the isolated cells.

119. (New) The method of claim 118, further comprising growing the pooled cells.

120. (New) The method of claim 19, wherein the plurality of different RNAs, or proteins encoded by the plurality of different RNAs, are selected from the group consisting of RNAs or proteins in the same or a related biological pathway, RNAs or proteins that act upstream or downstream of each other, RNAs or proteins that have a modulating,

activating or repressing function to each other, RNAs or proteins that are dependent on each other for function or activity, RNAs or proteins that are components of the same complex, and proteins from the same protein family.

121. (New) The method of claim 19 for isolating cells expressing two or more RNA expression libraries, comprising the steps of:

introducing into cells a plurality of DNAs encoding a first RNA expression library, wherein each DNA further encodes a first nucleic acid tag sequence, and wherein at least a subset of the plurality of DNAs encodes the same first nucleic acid tag sequence;

introducing into the cells a plurality of DNAs encoding a second RNA expression library, wherein each DNA further encodes a second nucleic acid tag sequence, and wherein at least a subset of the plurality of DNAs encodes the same second nucleic acid tag sequence;

exposing the cells to a first signaling probe that produces a detectable signal upon hybridization to said first nucleic acid tag sequence;

exposing the cells to a second signaling probe that produces a detectable signal upon hybridization to said second nucleic acid tag sequence; and

isolating the cells that produce both signals.

122. (New) The method of claim 19, wherein the nucleic acid tag sequence comprises multiple target sequences, wherein one signaling probe hybridizes to each target sequence.

123. (New) The method of claim 19, wherein the DNA encodes multiple nucleic acid tag sequences.
124. (New) The method of claim 19, wherein the DNA encoding said nucleic acid tag sequence is:
- (a) in frame with the DNA encoding said RNA; or
 - (b) out of frame with the DNA encoding said RNA.
125. (New) The method of claim 19, wherein the DNA further encodes a selection marker, and wherein the method further comprises the step of selecting the cells using the selection marker after introducing the DNA into the cells but prior to exposing said cells to the signaling probe.
126. (New) The method of claim 19, wherein said DNA is operably linked to a conditional promoter.
127. (New) The method of claim 126, wherein the RNA encoded by the DNA, or the protein encoded by the RNA, is lethal or damaging to the cell when expressed.
128. (New) The method of claim 126, further comprising the step of adding to the cells a compound that modulates the expression of said RNA or plurality of RNAs prior to the exposing step.

129. (New) The method of claim 19, wherein each DNA of said plurality of DNAs further encodes a second DNA sequence encoding a preselected RNA.
130. (New) The method of claim 129, wherein said plurality of DNAs encodes a plurality of variable test RNAs.
131. (New) A method of identifying a compound that activates a conditional promoter, comprising the steps of:
- adding a test compound to the cells isolated by the method of claim 126;
 - assaying for the presence of the second RNA under the control of the conditional promoter; and
 - identifying the test compound as a compound that activates the tissue specific promoter if the cell expresses the second RNA.
132. (New) A method of identifying a test RNA that activates a conditional promoter comprising the steps of:
- assaying for the presence of a second RNA under the control of the conditional promoter in cells isolated by the method of claim 126;
 - obtaining the cells that express the second RNA under the control of the conditional promoter; and
 - identifying the test RNA that activates the conditional promoter.

133. (New) The library of claim 103, wherein said library is generated by separately growing the plurality of cells to generate a plurality of separate cell lines.
134. (New) The library of claim 103, wherein said library is generated by pooling the plurality of cells and growing said pooled cells.
135. (New) The library of claim 103, wherein said plurality of different RNAs, or proteins encoded by the plurality of different RNAs, are selected from the group consisting of RNAs or proteins in the same or a related biological pathway, RNAs or proteins that act upstream or downstream of each other, RNAs or proteins that have a modulating, activating or repressing function to each other, RNAs or proteins that are dependent on each other for function or activity, RNAs or proteins that are components of the same complex, and proteins from the same protein family.
136. (New) The library of claim 103, wherein at least one of said DNAs encodes an antisense RNA, an shRNA, or an siRNA.
137. (New) The library of claim 103, wherein the nucleic acid tag sequence comprises multiple target sequences, wherein one signaling probe hybridizes to each target sequence.
138. (New) The library of claim 103, wherein at least one of said DNAs encodes multiple nucleic acid tag sequences.

139. (New) The library of claim 103, wherein the DNA encoding said nucleic acid tag sequence is:
- (a) in frame with the DNA encoding said RNA; or
 - (b) out of frame with the DNA encoding said RNA.
140. (New) The library of claim 103, wherein at least one of said DNAs further encodes a selection marker.
141. (New) The library of claim 103, wherein at least one of said DNAs is operably linked to a conditional promoter.
142. (New) The library of claim 141, wherein the RNA encoded by the DNA operably linked to a conditional promoter, or the protein encoded by said RNA, is lethal or damaging to the cell when expressed.
143. (New) The library of claim 103, wherein each DNA of said plurality of DNAs further encodes a second DNA sequence encoding a preselected RNA.
144. (New) The library of claim 103, wherein said library encodes a plurality of variable test RNAs.